

What is claimed:

- 5
1. A method of producing platelet derived growth factor (PDGF), comprising:
providing a transgenic mammal whose somatic and germ cells comprise a nucleic acid sequence encoding PDGF operably linked to a promoter which directs expression into mammary gland epithelial cells; and
obtaining milk from the transgenic mammal, wherein at least 30% of the PDGF in the milk is as a dimer.
 - 10 2. The method of claim 1, wherein the nucleic acid sequence encodes a PDGF A chain and at least 30% of the PDGF in the milk is as a PDGF-AA homodimer.
 3. The method of claim 1, wherein the nucleic acid sequence encodes a PDGF B chain and at least 30% of the PDGF in the milk is as a PDGF-BB homodimer.
 - 15 4. The method of claim 1, wherein the nucleic acid sequence comprises a nucleic acid sequence encoding a PDGF A chain and a nucleic acid sequence encoding a PDGF-B chain.
 - 20 5. The method of claim 4, wherein the nucleic acid sequence encoding the PDGF A chain and the nucleic acid sequence encoding the PDGF B chain are under control of the same promoter.
 6. The method of claim 4, wherein the nucleic acid sequence encoding the PDGF A chain is operably linked to a different promoter than the nucleic acid sequence encoding the PDGF B chain.
 - 25 7. The method of claim 1, wherein the transgenic mammal comprises a nucleic acid sequence encoding a PDGF A chain and a nucleic acid sequence encoding a PDGF B chain.
 - 30

8. A method of producing a transgenic mammal capable of expressing an active PDGF molecule in its milk, comprising
- introducing into a cell a nucleic acid sequence encoding a PDGF chains operably linked to a promoter which directed expression in mammary epithelial cells; and
- allowing the cell to give rise to a transgenic mammal, wherein the transgenic mammal expresses PDGF in its milk and at least 30% of the PDGF is present in the milk is in active form.

9. The method of claim 8, wherein the cell is an oocyte.

10. The method of claim 8, wherein the cell is a somatic cell, and the somatic cell or the nucleus of the somatic cell is introduced into an oocyte.

11. A method of producing a transgenic mammal capable of expressing an active PDGF molecule in its milk, comprising:
- introducing into a cell a nucleic acid sequence encoding a PDGF A chain operably linked to a promoter which directs expression in mammary epithelial cells;
- introducing into the cell a nucleic acid sequence encoding a PDGF B chain operably linked to a promoter which directs expression in mammary epithelial cells; and
- allowing the cell to give rise to a transgenic mammal, wherein the transgenic mammal expresses PDGF in its milk and at least 30% of the PDGF is present in the milk in active form.

12. The method of claim 11, wherein the cell is an oocyte.

13. The method of claim 11, wherein the cell is a somatic cell, and the somatic cell or the nucleus of the somatic cell is introduced into an oocyte.

14. A method of producing a transgenic mammal capable of expressing an active PDGF molecule in its milk, comprising:

providing a cell from a transgenic mammal whose germ and somatic cells comprise a nucleic acid sequence encoding a PDGF-A chain operably linked to a promoter which directs expression in mammary epithelial cells;

introducing into the cell a nucleic acid sequence encoding a PDGF-B chain operably linked to a promoter which directs expression in mammary epithelial cells; and

allowing the cell to give rise to a transgenic mammal, wherein the transgenic mammal expresses PDGF in its milk and at least 30% of the PDGF is present in the milk in active form.

5

10

15. The method of claim 14, wherein the cell is an oocyte.

16. The method of claim 14, wherein the cell is a somatic cell, and the somatic cell or the nucleus of the somatic cell is introduced into an oocyte.

15

17. A milk preparation obtained from a transgenic mammal whose genome contains a nucleic acid sequence encoding at least one PDGF chain operably linked to a promoter which directs expression in mammary epithelial cells, wherein the PDGF chain is expressed in the mammary epithelial cells the transgenic mammal and wherein at least 30% of the PDGF in the milk is present as a dimer.

20

18. The milk preparation of claim 17, wherein the PDGF chain is the PDGF A chain and at least 30% of the PDGF is present in the milk is as a PDGF-AA homodimer.

25

19. The milk preparation of claim 17, wherein the PDGF chain is the PDGF B chain and at least 30% of the PDGF is present in the milk is as a PDGF-BB homodimer

30

20. The milk preparation of claim 17, wherein the genome of the transgenic mammal comprises a nucleic acid sequence encoding a PDGF A chain under the control of a promoter which directs expression in mammary epithelial cells and a nucleic acid sequence encoding a PDGF B chain under the control of a promoter which directs expression in mammary epithelial cells.

21. The milk preparation of claim 20, wherein at least 30% of the PDGF present in the milk is as a PDGF-AB heterodimer.

22. The milk preparation of claim 17, wherein the PDGF is human PDGF.

23. The milk preparation of claim 17, wherein the transgenic mammal is a goat.

24. The milk preparation of claim 17, wherein the milk preparation comprises at least 1 mg/ml PDGF.

25. An isolated nucleic acid comprising a nucleic acid sequence encoding a biologically active PDGF or a homolog thereof operatively linked to a regulatory sequence capable of directing the expression of PDGF in the mammary gland of non-human transgenic mammals.

26. The nucleic acid of claim 25, wherein the nucleic acid sequence encodes a PDGF A chain.

27. The nucleic acid of claim 25, wherein the nucleic acid sequence encodes a PDGF B chain.

28. The nucleic acid of claim 26, wherein the nucleic acid sequence further encodes a PDGF B chain.

29. The nucleic acid of claim 25, wherein the nucleic acid sequence coding for PDGF is mono- or dicistronic.

30. The nucleic acid of claim 25, wherein the nucleic acid sequence is dicistronic.

31. The nucleic acid of claim 25, wherein the nucleic acid comprises the expression cassette BC701 or BC734.

30

add (B1)